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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/269,250	05/21/1999	ELSA AFRA, JULIA, MARIA GOULMY	2799/58994	9675

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EXAMINER
SOUAYA, JEHANNE E

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/269,250	Applicant(s) GOULMY, ELSA AFRA, JULIA, MARIA	
	Examiner Jehanne Souaya	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 May 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Currently, claims 1-20 are pending in the instant application. Claims 18-19 are withdrawn from consideration as being drawn to non elected inventions and claim 20 is newly added. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following rejections are newly applied (necessitated by amendment) or are reiterated (it is noted that the rejection of newly added claim 20 will be addressed under the heading "Maintained Rejections"). They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The rejection of claim 1 under 35 USC 112/2nd paragraph for the recitation of "HA-1 antigen" is withdrawn. The rejection was made on the grounds that the examiner could not determine, based on the definitions provided in the specification, whether "HA-1 antigen' referred to the nonapeptide VLXDDLLEA or to a larger sequence. Upon reading applicants response, the examiner concluded that "HA-1 antigen" refers to a sequence, larger than the nonapeptide, that has not been disclosed in the specification.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Maintained Rejections

Claim Rejections - 35 USC § 112

Written Description

4. Claims 1-17 and newly added claim 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to typing alleles of the minor histocompatibility antigen HA-1 comprising detecting polymorphic nucleotides in the cDNA or genomic nucleic acids of the alleles. However, the specification does not provide sufficient written description as to the sequence of the HA-1 antigen, or the cDNA or genomic DNA that encodes the full HA-1 antigen. The specification teaches allele typing of the HA-1 peptide which is disclosed as SEQ ID NO 17. Two alleles are present resulting from a sequence change at nucleotide position 8 of SEQ ID NO 17 (nucleic acid sequence that encodes the HA-1 peptide), the "R" allele (SEQ ID NO 17) and the "H" allele (SEQ ID NO 19) corresponding to an Arginine or a Histidine at the 3rd position of the HA-1 nonapeptide (VLXDDLLEA, where X is either arginine or histidine). The specification teaches that typing these two alleles is important in typing potential donors for bone marrow transplants to prevent Graft versus Host Disease (GVHD), as patients, from two families, receiving bone marrow transplants from HLA identical donors within the family were found to develop GVHD. The specification teaches that allele typing of the HA-1 nonapeptide showed

that donors and recipients differed in the HA-1 allele (p 21, example 1). The specification fully teaches the skilled artisan how to type the "H" or the "R" allele in a subject and teaches the sequence of the HA-1 peptide (SEQ ID NO 17 or 19) (see figure 5, p. 5-6). The specification further teaches that the HA-1 peptide is encoded by 2 exons from the KIAA0223 gene (p 6 and 7), and teaches the sequence of the intron located between these two exons (SEQ ID NO 1). The specification, however does not teach the full sequence of the HA-1 *antigen*, nor does the specification teach the cDNA or genomic DNA that corresponds to the nucleic acid sequences that encode the antigen. The specification teaches that the KIAA0223 gene encodes the HA-1 antigen, but does not disclose what sequences within the KIAA0223 gene correspond to the HA-1 gene. It cannot be determined from the disclosure in the specification if the gene product of the KIAA0223 gene is the HA-1 *antigen*, wherein the HA-1 peptide is a peptide located withing the HA-1 antigen (The specification does not teach that the KIAA0223 gene is the HA-1 gene) or whether the complete sequence of the HA-1 antigen is the HA-1 nonapeptide (SEQ ID NOS 17 or 19) as the specification states that The GvHD associated mH antigen HA-1 is a nonapeptide derived from the di allelic KIAA0223 gene (p. 21). As the claims are drawn to typing unidentified alleles in undisclosed sequences, and the specification does not adequately describe the breadth of these undisclosed sequences, each of the claimed inventions is a genus for which a representative number of species for each genus must be disclosed to meet the written description requirement of 112, first paragraph. As set forth by the Court in *Vas Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable

clarity" that as of the filing date applicant was in possession of the claimed invention. Absent a written description disclosing the full sequence of the HA-1 antigen (if the HA-1 peptide does not represent the full sequence of the HA-1 antigen) or the sequences of the KIAA0223 gene that correspond to the cDNA or genomic sequences that encode the HA-1 antigen (if the HA-1 peptide does not represent the full sequence of the HA-1 antigen), the specification fails to show that applicant was, in fact, "in possession of the claimed invention" at the time the application for patent was filed.

With regard to claim 13, the claim is broadly drawn to an isolated nucleic acid displaying "80% sequence homology" to SEQ ID NO 1, 17 or 18 or any fragment that can be used for HA-1 typing. Many sequences are encompassed by applicant's claims, and particularly those having "80 % sequence homology" or any fragment of such would bear little resemblance to the single HA-1 peptide (VLXDDLLEA) and intronic sequence (SEQ ID NO 1) taught in the specification. Neither the claims nor the specification set forth any structural or functional characteristics that a skilled artisan could use to identify such polynucleotides other than by SEQ ID NO1. Further, with regard to newly added claim 20, such a claim encompasses undisclosed sequences including genomic sequences, and a large number of variants, mutants, and homologs of SEQ ID NOS 1, 17, and 18 that have not been taught or described in the specification. Each of the claimed inventions is a genus for which a representative number of species for each genus must be disclosed to meet the written description requirement of 112, first paragraph. As set forth by the Court in *Vas Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, the written description must convey to

one of skill in the art "with reasonable clarity" that as of the filing date applicant was in possession of the claimed invention.

Response to Arguments

The response traverses the rejection. The response traverses that the claimed invention is drawn to a method or kits for typing of alleles and that fore these claims, the inventor should be required to show that at the moment of invention, the inventor was able to discriminate between alleles. This argument has been thoroughly reviewed but was found unpersuasive as the invention is drawn to typing of alleles in sequences that have not been taught or described in either the specification or the art, at the time the instant application was filed. Therefore, the specification fails to show that applicant was "in possession" of these undisclosed essential sequences. Consequently, since a description of the sequences is lacking, a description of typing alleles to these undisclosed sequences is also lacking. The claims are drawn to methods of detecting undisclosed variations in undisclosed sequences.

The response further traverses that with regard to claims 11-14, the claims are concerned with nucleic acids that can be found with the information given in the specification and that applicant should not be required to exhaustively list all possible variations. This argument has been thoroughly reviewed but was found unpersuasive. Firstly, the claims in question (11-12 and 14) are not drawn to any specific sequence and are drawn to sequences for use in a method that uses undisclosed sequences. For example, it is unclear how the skilled artisan would be able to determine the sequence of a primer if the target sequence (in other words, the sequence it

hybridizes to) is not disclosed, other than by SEQ ID NO. Such a recitation is essential in determining the specific sequence of a primer or a probe. With regard to such, it is noted that the art does not teach the skilled artisan what the exact sequence of a primer *is* if the sequence it hybridizes to is unknown. Further, claims 11 and 12 only recite "a [primer or probe] for use in a method according to claim..." No structural language is presented in the claims such that a correlation can be made with regard to the use of such oligonucleotides in a method "for typing of alleles of the Minor Histocompatibility Antigen HA-1". Secondly, while the specification discloses some specific sequences that can be used in the method of claim 1, such sequences are not representative of the large genus of alleles and sequences encompassed by the claimed invention.

With regard to claim 13, the response asserts that the examiner assertion that the claim lacks any functional characteristics that a skilled artisan could use to identify polynucleotides other than by SEQ ID NO is inaccurate since the claim recites "used as a primer or as a probe for HA-1 typing". This argument has been thoroughly reviewed but was found unpersuasive. Firstly, it is noted that the claim's purported functional language is unclear in that the sequence of the HA-1 antigen is not disclosed in the specification. Therefore, without such, the skilled artisan would not be able to determine whether a sequence could be used for HA-1 typing. Secondly, it is unclear how the term "identified" relates to the length of the sequences in question as well as to any variations in such sequences. It is noted that this issue was also addressed in the previous office action under 35 USC 112, 2nd paragraph. It is unclear if the term is meant to

encompass a sequence "consisting" of a specific SEQ ID NO, a sequence "comprising" a specific SEQ ID NO, or a sequence that can hybridize to a specific SEQ ID NO. Further, the claim is drawn to polynucleic acid sequences displaying 80% homology to SEQ ID NO 1, 17, or 18 or to sequences that have 80% homology to fragments of SEQ ID NOS 1, 17, 18. As noted in the previous office action, many sequences are encompassed by applicant's claims which would bear little resemblance to the sequences taught in the specification. Without a disclosure of a representative number of HA-1 alleles encompassed by the claims, the skilled artisan would not be able to determine whether sequence could be "used as a primer or as a probe for HA-1 typing". With regard to newly added claim 20, such a claim encompasses undisclosed sequences including genomic sequences, and a large number of variants, mutants, and homologs of SEQ ID NOS 1, 17, and 18 that have not been taught or described in the specification. Such a claim also encompasses a broader genus than that of claim 13, and as in claim 13, the disclosure of the single intron (SEQ ID NO 1) and nonapeptide (SEQ ID NO 17) is not representative of the large number of sequences encompassed by the presently claimed application. With the exception of "an isolated nucleic acid consisting of SEQ ID NOS: 1 and 17", the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18

USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

Indefinite

5. Claims 2, 4, and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 4, and 9 are indefinite as these claims refer to multiple SEQ ID NOS that include both nucleotide and amino acid sequences. Thus it is unclear with regard to claim 2, how nucleic acid sequences (SEQ ID NOS 17 and 19) correspond to "comprising amino acids in sequence as shown in SEQ ID NOS 17-20". With regard to claims 4 and 9, it is unclear if "position 4 or position 8" refers to a nucleic acid or a amino acid sequence.

Conclusion

6. No claims are allowable. It is noted that newly amended claim 17 is improperly multiply dependent. See MPEP § 608.01(n).

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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Jehanne Souaya
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Patent examiner
Art Unit 1634
June 20, 2002